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GONADOTROPHIC HORMONE AND CORTISOL LEVELS IN WOMEN DURING ADAPTATION TO POLAR CONDITIONS

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An important role in adaptive changes in homeostatic systems supporting life and work under conditions of the Far North is played by hormones. For instance, the importance of catecholamines and corticosteroids in mobilization of energy reserves and, in particular, in the switch from a carbohydrate to a fat type of metabolism, has been demonstrated [1, 2]; changes have been noted in thyroid and pancreatic insular hormone secretion in the course of human adaptive reactions [3]. The role of other hormones in adaptive changes has not yet been adequately studied. There is indirect evidence that hormones of the reproductive system also participate in these processes. For instance, habituation to the climatogeographic conditions beyond the Arctic Circle in 20% of women immigrants has been shown to be accompanied by hormonal disturbances, manifested as an increased frequency of amenorrhea, anovulatory cycles, and functional sterility [4]. However, no direct mention of any change in the levels of reproductive hormones in connection with adaptive reactions could be found in the accessible literature.

The aim of this investigation was to study the time course of levels of pituitary gonadotropic hormones and also of the adrenocortical hormone cortisol, during adaptation to conditions of the Far North in inhabitants of Magadan Region.

METHOD

Altogether 307 healthy women aged from 20 to 29 years, with a regular menstrual cycle during the last 6 months, were studied. None of the subjects was taking hormonal contraceptives and none had undergone abortion during the past year. The duration of the menstrual cycle varied from 26 to 32 days. Its phase was determined from the history, since most of the subjects kept diaries. Ovarian cycles lasting 27 days were treated as 26-day, and those lasting 29 days as 28-day cycles. Since according to the results of previous investigations [5, 6] the ovulatory peak of luteinizing hormone (LH) and the increase in follicle-stimulating hormone (FSH) level which coincided with it in most cases, were observed between the 12th and 17th days of the menstrual cycle, the subjects included some women whose menstrual cycle did not fall within this period, i.e., the phase of conjectural ovulation was deliberately excluded from the study. In the case of short (26-day) cycles, days from the 9th through the 15th were excluded. The beginning of the cycle was counted from the 1st day of menstruation (which was excluded).

Depending on the duration of their stay in Magadan Region the subjects were divided into the following groups: 0) Chukchi and Eskimos, inhabitants of the Chukotka Autonomous Territory (in the town of Anadyr') — 71 persons; group I) women born in Magadan Region (first generation immigrants) — 75; group II) women immigrating from the Central Regions of the country who had lived in Magadan Region for up to 3 years — 79; group III) women immigrants who had lived from 4 to 9 years in Magadan — 90; group IV) women who lived over 10 years in Magadan Region — 83.

Blood was taken between 9 and 11 a.m. local time and the plasma was frozen and kept at −20°C. LH, FSH, and cortisol were determined by radioimmunoassay, using standard LHK-PR, FSHK-PR, and CORCTK-125 kits. The investigation was conducted in the fall and winter (October-February). The results were subjected to statistical analysis. The coefficient of correlation was calculated to determine dependence between hormone levels.

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TABLE 1. Characteristics of Menstrual Cycle (duration) in Women Studied

Criteria	Group				
	0	I	II	III	IV
Mean duration of cycle in days ($\bar{x} \pm s_{\bar{x}}$)	29,21±0,24	28,49±0,3	28,38±0,65	28,63±0,4	27,82±0,44
Percentage of 26-day cycles	—	29,41	23,07	9,37	37,5
Percentage of 28-day cycles	46,34	41,17	30,77	40,62	31,2
Percentage of 30-32-day cycles	53,66	29,41	46,15	50,0	31,8

TABLE 2. Peripheral Blood Hormone Levels in Women Studied

Hormones	Cortisol	Peripheral blood hormone concentration, ng/ml ($\bar{x} \pm s_{\bar{x}}$) for undermentioned				
		0	I	II	III	IV
LH	Folliculin	3,03±0,38 (n = 39)*	4,63±1,08 (n = 38)	5,12±0,74 (n = 38)	3,14±0,35 (n = 43)	3,2±0,72 (n = 31)
	Lutein	3,22±0,58 (n = 32)	5,04±1,0 (n = 37)	6,04±1,33 (n = 41)	4,19±0,63 (n = 47)	5,07±1,06 (n = 42)
FSH	Folliculin	2,59±0,4 (n = 39)	2,47±0,3 (n = 38)	1,98±0,24 (n = 38)	3,31±0,52 (n = 43)	3,59±0,72 (n = 31)
	Lutein	1,39±0,15 (n = 32)	2,01±0,49 (n = 37)	2,19±0,54 (n = 41)	2,59±0,38 (n = 47)	1,6±0,19 (n = 42)
Cortisol	Folliculin	354,27±45,22 (n = 20)	207,8±29,6 (n = 20)	149,72±13,72 (n = 22)	120,64±22,58 (n = 24)	115,07±14,96 (n = 23)
	Lutein	314,42±39,77 (n = 19)	135,0±12,25 (n = 22)	166,4±45,16 (n = 20)	154,5±21,82 (n = 20)	97,45±15,1 (n = 21)

Legend. *In parentheses n gives number of persons studied.

EXPERIMENTAL RESULTS

Group 0. The duration of the menstrual cycle was 28 to 32 days (mean 29.21 ± 0.2 days) and for the majority the cycle lasted 30-32 days (Table 1).

None of the women of the indigenous population studied has a cycle shorter than 28 days. The FSH concentration was a little higher (Table 2) in the folliculin than in the lutein phases of the cycle (2.59 ± 0.4 ng/ml compared with 1.39 ± 0.15 ng/ml); the LH level, on the other hand, was higher in the lutein (3.22 ± 0.58 ng/ml compared with 3.08 ± 0.38 ng/ml) phase, but the difference was not significant.

The amplitude of fluctuations of LH levels in different individuals was 6.17 ($x_{max} - x_{min} = 7.25 - 1.08$), and that of FSH was 4.62 ($x_{max} - x_{min} = 5.42 - 0.80$). In the lutein phase of the cycle predominantly low values for LH and FSH were found (Figs. 1B and 2B). No correlation was found between the gonadotrophic hormone levels.

The plasma cortisol concentration was high: 314.42 ± 39.77 ng/ml in the lutein phase and 354.27 ± 45.22 ng/ml in the folliculin phase. In most cases the cortisol level exceeded 180.0 ng/ml (Fig. 3: A, B). In the folliculin phase of the cycle positive correlation was observed (Table 3) between the levels of gonadotrophic hormones and cortisol ($p < 0.05$).

Group I. The duration of the menstrual cycle of women born in Magadan Region was 28.49 ± 0.3 days (variations from 26 to 32 days); nearly half (41.17%) of the women had a cycle of 28 days. Some shortening of the cycle (not statistically significant) compared with the previous group of subjects was evidently connected with the high proportion of subjects with a 26-day cycle (29.41%).

Correlation between the gonadotrophic hormones was analyzed in accordance with a general principle: The LH concentration was a little higher (not significantly) in the lutein phase of the menstrual cycle (5.04 ± 1.0 and 4.63 ± 1.08 ng/ml in the lutein and folliculin stages respectively), whereas the FSH concentration was higher in the folliculin phase (2.47 ± 0.3 ng/ml compared with 2.01 ± 0.49 ng/ml). The higher LH level in the women of this group than in the indigenous population and was not statistically significant. In the following phase

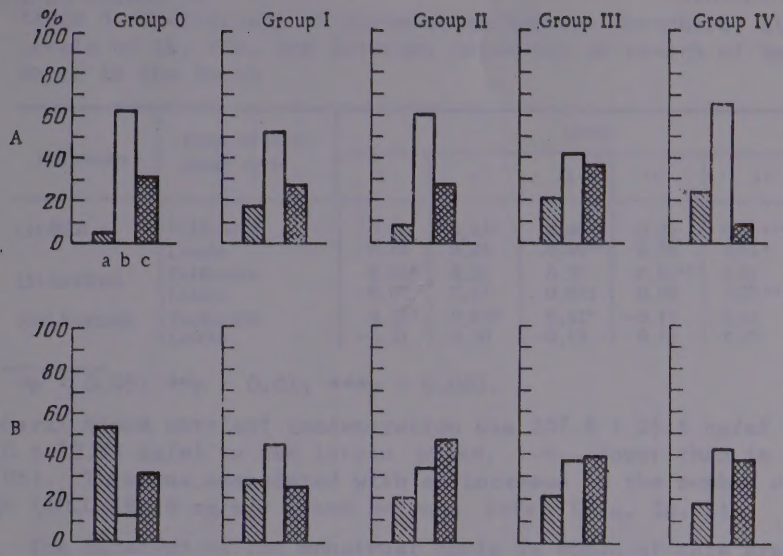


Fig. 1. Relative blood LH levels in folliculin (A) and lutein (B) phases of menstrual cycle. Legend: a) persons with hormone concentration below 2 ng/ml, %; b) persons with hormone concentration of 2-4 ng/ml, %; c) persons with hormone concentration above 4 ng/ml, %.

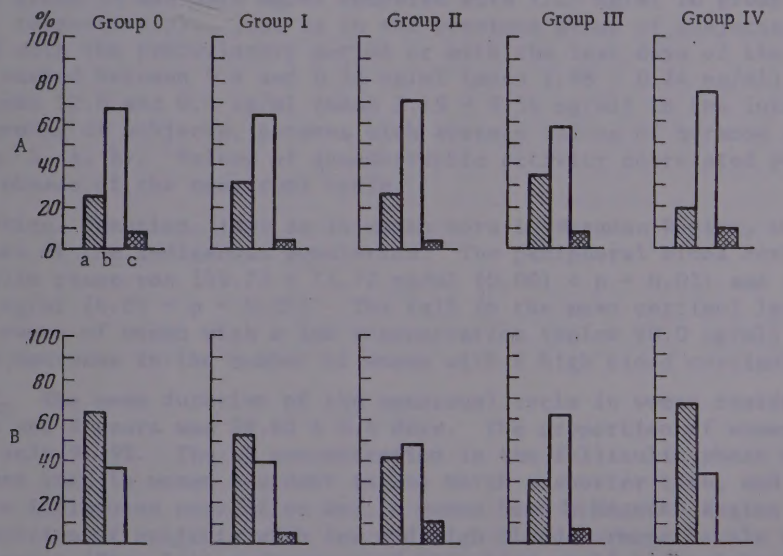


Fig. 2. Relative blood FSH levels in folliculin (A) and lutein (B) phases of menstrual cycle. Legend: a) persons with hormone concentration below 1.5 ng/ml, %; b) persons with hormone concentration of 1.5-5.0 ng/ml, %; c) persons with hormone concentration above 5.0 ng/ml, %.

of the cycle positive correlation was observed between the basal levels of gonadotrophic hormones ($p < 0.05$). The high values of LH secretion (from 9.4 to 19.0 ng/ml) observed in some women in the folliculin phase were evidently not connected with the preovulatory rise of the hormone level, for this occurred on the 3rd, 5th, and 6th days from the beginning of menstruation in 28-30-day cycles. In the lutein phase of the cycle a very high LH level (from 9.0 to 21.0 ng/ml) was recorded on the 19th-24th days of the cycle, whose duration was 28 days.

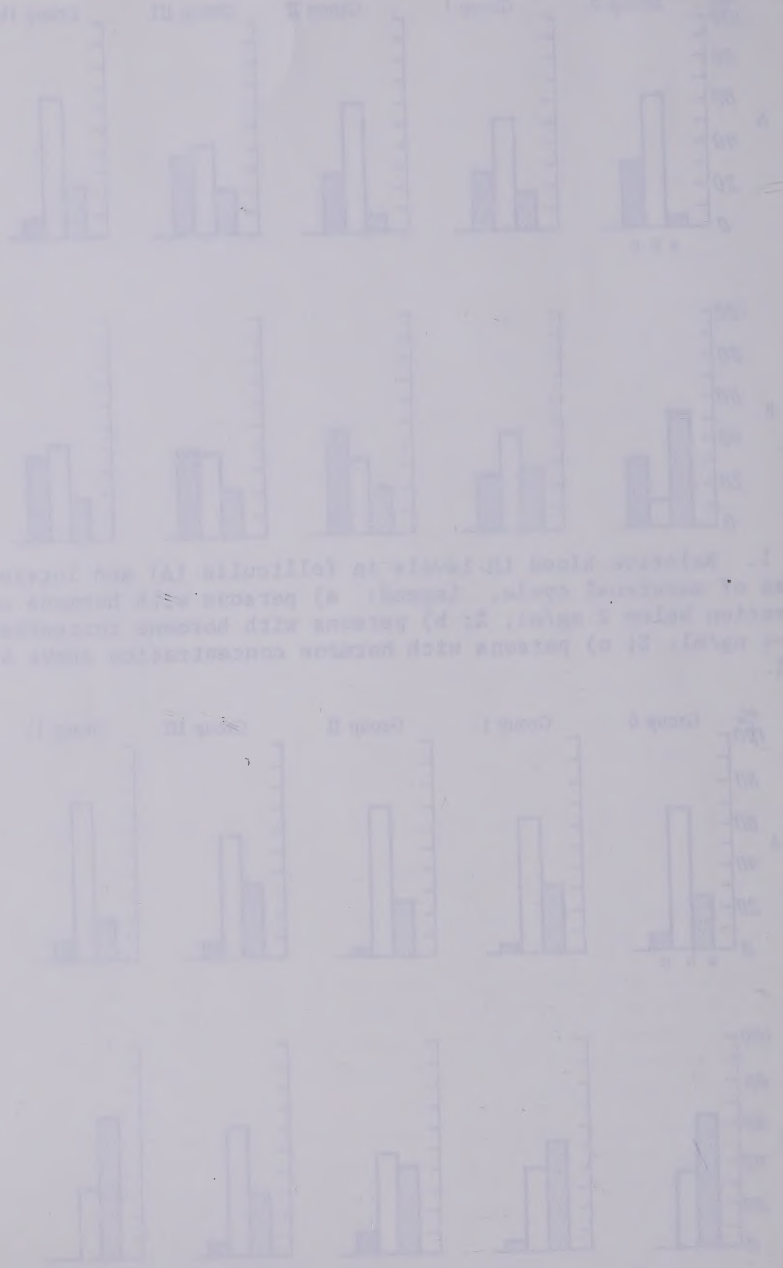


TABLE 3. Coefficient of Correlation Between Peripheral Blood Levels of LH, FSH, and Cortisol Depending on Length of Residence in the North

Hormones	Phase of menstrual cycle	Group				
		0	I	II	III	IV
LH/FSH	Folliculin	0,1	0,43*	0,64**	0,22	0,86***
	Lutein	0,15	0,05	0,49**	0,31	0,53*
LH/cortisol	Folliculin	0,65*	0,26	0,26	0,67**	0,03
	Lutein	—0,07	0,17	—0,032	0,09	0,75**
FSH/cortisol	Folliculin	0,59*	0,049	0,42*	—0,11	—0,32
	Lutein	—0,21	0,20	—0,13	0,15	0,32

*$p < 0.05$; **$p < 0.01$; ***$p < 0.001$.

The peripheral blood cortisol concentration was 207.8 ± 29.6 ng/ml in the folliculin stage and 135.0 ± 12.25 ng/ml in the lutein phase, i.e., lower than in the previous group ($0.01 < p < 0.05$). This was associated with an increase in the number of subjects with a moderately high (60.0-180.0 ng/ml) blood hormone level (Fig. 3A, B).

Group II. The duration of the menstrual cycle in women of this group was 28.38 ± 0.65 days; the most frequent duration of the cycle (46.15%) was 30-32 days; only 23.07% of women had short cycles. The mean values of LH secretion in the folliculin phase of the cycle (5.12 ± 0.74 ng/ml) and in the lutein phase (6.04 ± 1.33 ng/ml) were higher than in Chukchi and Eskimo women (in the first half of the cycle the difference has statistically significant ($p < 0.05$) on account of higher blood hormone levels compared with the indigenous inhabitants (x_{max} in group II was 39.0 ng/ml compared with 7.25 ng/ml in group 0; x_{min} was 1.95 and 1.05 ng/ml respectively). Just as in the previous group of subjects high LH levels were not associated with the preovulatory period or with the last days of the corpus luteum phase. The FSH level varied between 5.4 and 0.54 ng/ml (mean 1.98 ± 0.24 ng/ml) in the folliculin phase and between 12.0 and 0.4 ng/ml (mean 2.19 ± 0.54 ng/ml) in the lutein phase; unlike in two previous groups of subjects, persons with average values of hormone concentration predominated (Fig. 2, A, B). Values of gonadotrophic activity correlated positively with each other in both phases of the menstrual cycle.

Adrenocortical function, just as in women born in Magadan Region, was significantly lower than in women of the indigenous population: The peripheral blood cortisone concentration in the folliculin phase was 149.72 ± 13.72 ng/ml ($0.001 < p < 0.01$) and in the lutein phase 166.4 ± 45.16 ng/ml ($0.01 < p < 0.05$). The fall in the mean cortisol level was associated with the appearance of women with a low concentration (below 60.0 ng/ml) of the hormone (Fig. 3A) and with a decrease in the number of women with a high blood cortisol level (Fig. 3, A,B).

Group III. The mean duration of the menstrual cycle in women resident in Magadan Region between 4 and 9 years was 28.63 ± 0.4 days. The proportion of women with short cycles (26 days) was only 9.39%. The LH concentration in the folliculin phase was significantly ($p < 0.05$) lower than in women resident in the North a shorter time, and it was close to that observed in the indigenous population and in women born in Magadan Region (3.14 ± 0.35 ng/ml). Since the proportion of subjects with low and high blood hormone levels was increased under these circumstances (Fig. 1A), a decrease of this kind could be explained by the lower values of LH concentration. In fact, x_{max} in this group was 7.4 ng/ml and x_{min} was 0.9 ng/ml. In the second half of the cycle, besides the factors mentioned above, a reduction in the contribution of high LH concentrations, accompanied by a simultaneous increase in the contribution of low hormone levels also played a role. The FSH level, on the contrary was significantly ($p < 0.01$) increased compared with the previous group of subjects in the folliculin phase (3.31 ± 0.52 ng/ml), and this could be attributed to the higher values of hormone secretion in the women of this group ($x_{max} - x_{min} = 11.0 - 0.22$ ng/ml).

Adrenal function remained at the same level as in the previous group (Table 2). The group of subjects with a low cortisol level was reduced (and in the lutein phase it disappeared) (Fig. 3, A, B). Positive correlation was found between the FSH and cortisol levels (Table 3).

Group IV. The duration of the menstrual cycle in women of this group was 27.82 ± 0.4 days, i.e., some shortening of the cycle was observed compared with previous groups, and this

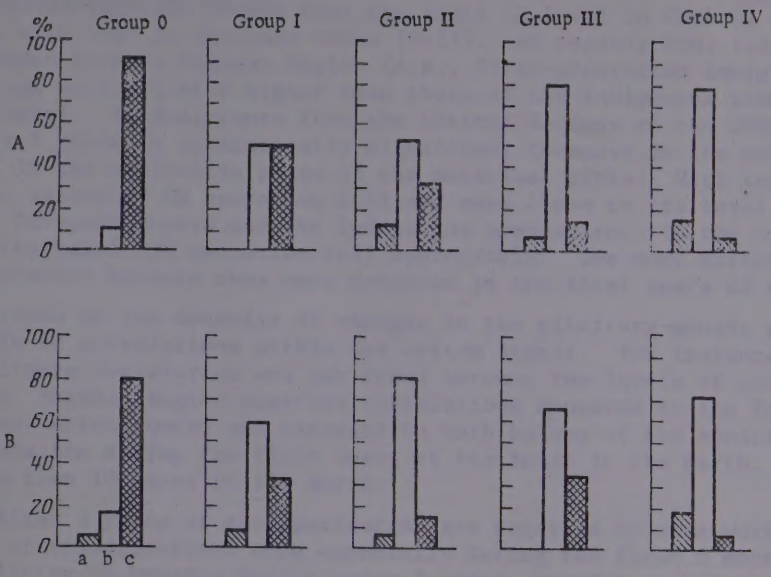


Fig. 3. Relative blood levels of cortisol in folliculin (A) and lutein (B) phases of menstrual cycle. Legend: a) persons with hormone concentration below 60.0 ng/ml, %; b) persons with hormone concentration of 60.0-180.0 ng/ml, %; c) persons with hormone concentration above 180.0 ng/ml, %.

)uld be explained by the considerable proportion of subjects with a short ovarian cycle 37.5%). Basal secretion of gonadotrophic hormones was at the same level as in women with shorter period of residence in the North (Table 2), and only the level of FSH secretion in ıe corpus luteum phase was lower ($p < 0.05$). This last fact can be explained by the sharp ıcrease in the number of subjects with a low FSH concentration (Fig. 2B). Individual fluctuaions in the peripheral blood levels of gonadotrophic hormones were increased (for LH $x_{max} - x_{min} = 19.0 - 0.9$ ng/ml; for FSH $x_{max} - x_{min} = 19.08$ ng/ml. Compared with the previous group)sitive correlation was strengthened between the levels of the two gonatrophic hormones, es-ecially in the folliculin phase of the cycle.

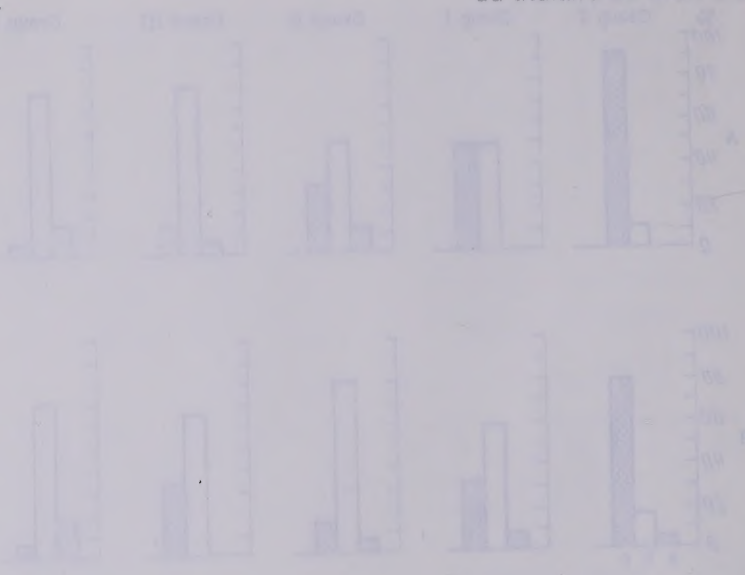
The mean blood cortisol levels were lower than in all previous groups of immigrant women Table 2) on account of a decrease in the number of persons with a high cortisol level and a multaneous increase in the number of persons with a low blood hormone concentration (Fig. A, B).

DISCUSSION

According to modern views on the mechanisms of adaptation to new environmental condi-ons and, in particular, to the unfavorable factors of polar regions, the role of trigger paratus, enabling mobilization of energy and structural reserves on their oriented trans-ssion to the dominant system responsible for adaptation, is ascribed to the endocrine sys-m [7]. Having completed the reprogramming of the effector systems in accordance with the ternal situation, the hormonal system reduces its activity [8].

The duration of this reprogramming may vary within wide limits. It must also be taken into nsideration that these hypotheses are based mainly on reactions of the pituitary-adreno-rtical system and the sympathoadrenal system, without consideration of the state of other docrine complexes.

The present investigations was conducted on healthy young women with no signs of distur-nces of specific gynecological functions. That is why shifts in the hormonal balance, dis-vered in these subjects, could be ascribed mainly to nonspecific modifications characteriz-g to some degree the state of adaptation of women to conditions of the Far North. The re-lts of investigations of different groups of the immigrant population were compared with e same characteristics of pituitary gonadotrophic function in members of the indigenous pulation, relatively well adapted to the local climatogeographic conditions.



The investigations showed that the basal LH level in Chukchi and Eskimos was virtually identical with that in European women [9-11]. As regards FSH, its level was found to be lower. In women born in Magadan Region (i.e., first-generation immigrant population) values of LH secretion were a little higher than those of the indigenous inhabitants, but FSH was at the same level. In immigrants from the Central Regions of the USSR residing in Magadan Region under 3 years, a statistically significant increase in the peripheral blood LH level was found in the folliculin phase of the menstrual cycle. With lengthening of residence in the North, values of LH secretion fell and came close to its level in women from the Central Region of European Russia and the indigenous population. In the first 3 years after immigration, the basal FSH secretion fell appreciably. The most marked changes in the gonadotrophic hormonal balance thus were detected in the first years of residence in the Far North.

Our ideas on the dynamics of changes in the pituitary-gonads system were supplemented by analysis of correlations within the system itself. For instance, whereas in the indigenous inhabitants correlation was not found between the levels of gonatropic hormones, in women born in Magadan Region positive correlations appeared in the folliculin phase. This correlation was strengthened and extended to both halves of the menstrual cycle in the immigrant population during the first years of residence in the North, and also in women who had lived more than 10 years in the North.

The first 3 years of acclimatization are regarded by some workers as a period of manifestation of disadaptation, more especially during the first 6 months [12]. Among the group of women living in Magadan Region under 3 years, besides marked changes in the mean level of gonadotrophic hormones, considerable fluctuations also were observed in the hormone concentration, which evidently reflected individual differences in adaptive reactions of the woman to unusual conditions; strengthening of positive correlations within the gonadotrophic system, however, was evidence in our view of active and synchronous changes in the hormonal balance of nonspecific character.

In the subsequent period of residence in the North, which can be regarded as a relatively stable state, the need to maintain such correlations disappears, only to reappear in persons residing under these unfavorable conditions longer than 10 years, i.e., in the period of exhaustion of the reserves capacity of the body and the switching of control systems to a new level of functions.

It is generally known that an important role in increasing the resistance of the body to extremal environmental factors is displayed by the pituitary-adrenocortical system. The view has recently been expressed, on the basis of data on short-term and at times very small functional changes affecting the adrenal cortex [13-16], that activation of the adrenal cortex during acclimatization is necessary for only a short period [8].

A noteworthy feature of the present investigation was the high peripheral blood cortisol level in Chukchi and Eskimos. It is not yet clear why adrenocortical activity should be so high in the inhabitants of the Chukotka Autonomous Territory. In the immigrant population, including those born in Magadan Region, cortisol secretion was significantly lower than in women of the indigenous population. If the level of cortisol secretion to some degree characterizes the degree of strain on adaptive processes, it must evidently be postulated that adrenocortical hormones not only determine the choice of adaptive metabolic program of the body, but also help to maintain a relatively stable state of adaptation. However, to judge from the tendency for the blood cortisol concentration to fall in the immigrant population as their length of residence in the North increases, this role gradually diminishes.

CONCLUSION

The absolute LH and FSH concentrations in women of the different groups studied varies within quite narrow limits, and this may give the impression of insignificance of hormonal adaptive changes. Meanwhile these adaptive changes concern the endocrine system as a whole, suggesting a change in the hormonal background profile during adaptation to conditions of the Far North [3, 17], inevitably followed by metabolic reorganizations. However, the character of the consequences of the changes discovered is difficult to assess. It can also be concluded that the duration of adaptive hormonal fluctuations in persons exposed to polar conditions is very long and may exceed the lifespan of a single generation.

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